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Differences in the expression of epidermal growth factor receptor in lymph node metastases and primary tumors of the head and neck

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Purpose: An overexpression of the epidermal growth factor receptor (EGFR) has been found in a wide variety of malignancies including squamous cell carcinomas of the head and neck. The overexpression of EGFR is of increasing interest because of a possible contribution to metastasis. Primary tumors and metastasis may differ in the expression of EGFR and provide a basis for metastasis.

Methods: This study examined the expression of the cell-surface EGFR in frozen tissue samples from 30 primary carcinomas of the head and neck and from 30 lymph node metastases. The examination employed the use of an immunfluorescence assay using a mouse monoclonal antibody for localisation of immunoreactive EGFR.

Results: We saw a significant higher expression of EGFR in metastases than in primary tumors ($p = 0.005$). Examining the primaries, no correlation was seen between EGFR level and TNM-stage. We found an interesting correlation between EGFR level and histologic grading, immunoreactivity being significantly higher in G3 than in G1–G2 tumors ($p = 0.001$).

Conclusion: EGFR system may play an important role in the process of metastasis and elevated EGFR level might characterize more metastatic tumors. The significant correlation between EGFR level and the histologic grading suggests that EGFR expression may identify biologically more aggressive tumors.

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Oral squamous cell carcinoma (OSCC) – The role of to the tumor associated proteases uPA, PAI-1, cathepsin D, cathepsin B, cathepsin L and the receptor uPA-R

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Purpose: The pathway of plasmin activation is linked to tumor invasion and metastasis. The cascade of activation of cathepsin D, B, L and uPA, which is bound to its receptor uPA-R, induces plasmin which degregades the extracellular matrix and thus enables tumor invasion and metastasis. uPA is inactivated by PAI-I. Studies on various types of cancer proved the prognestic value of these proteases. Prospectively we determined the concentrations of uPA, uPA-R, PAI-1, cathepsin D, B and L.

Methods: From 220 patients with OSCC primary tumor- and benign tissue-specimen were taken. In these specimens (Triton X-100-extracts) concentrations of uPA, uPAR, PAI-1, cathepsins D, B and L were determined by ELISAs.

Results: Comparing intraindividually the concentration of proteases in malignant and benign tissue, in tumor specimen uPA-concentration was 20 times higher than in benign tissue, PAI-1 concentration was 6 times higher ($p < 0.0006$). Currently the measurements of uPAR, cathepsin D, cathepsin B and cathepsin L are evaluated.

Conclusion: The data indicates that uPA and PAI-1 could be of prognostic value in OSCC. In the next future the clinical and prognostic impact of these proteases for planning an individual oncological therapy has to be evaluated. The pathway of plasminogen activation could become a new strategy in the treatment of OSCC.

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Chromosomal alterations associated with malignancy in head and neck cancer

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Purpose: To discover molecular genetic alterations underlying the progression of head and neck squamous cell carcinomas (HNSCC) we performed Comparative Genomic Hybridization (CGH) on 50 primary tumors.

Methods: In CGH, equal amounts of differently labeled tumor DNA and normal reference DNA were hybridized simultaneously to normal metaphase chromosomes. They were visualized by different fluorochromes and the signal intensities were quantitated separately as gray levels along the single chromosomes. The over- and underrepresented DNA segments were determined by computation of ratio images and average ratio profiles.

Results: Prevalent changes observed in more than 50% of the HNSCC included deletions of chromosomes 1p, 4, 5q, 6q, 8p, 9p, 11, 13q, 18q and 21q and DNA overrepresentations of 11q13 as well as 3q, 8q, 16p, 17q, 19, 20q and 22q. The calculation of ratio profiles of tumor subgroups revealed that well differentiated carcinomas (G1) were defined by the deletions of chromosomes 3p, 5q and 9p together with the overrepresentation of 3q, suggesting the association with early tumor development. Accordingly, the undifferentiated tumors (G3) were characterized by additional deletions of chromosomes 4q, 8p, 11q, 13q, 18q, 21q and overrepresentations of 1p, 11q13, 19 and 22q.

Conclusion: Our data indicate that the CGH patterns of chromosomal imbalances may help to define the malignant potential of head and neck squamous cell carcinomas.

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Clinical and microbiological evaluation of radiotherapy (RT) induced mucositis in head and neck cancer patients

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Patients receiving curative radiotherapy (dose >66 Gy) were examined before, weekly during the course of RT and after RT. The extent of mucositis was recorded. Oropharyngeal bacterial flora was sampled before RT and regularly during the course using the oral rinse method. As mucositis prophylaxis patients used chlorhexidinegluconat 0.1% mouthrinse.

8.3% had cultures positive for yeast before RT, and 29.2% at the end of RT. 8 weeks after RT 33.3% were positive for yeast. Among patients who developed cultures positive for yeast at any time during the testperiod (62.5%), only 20% had received prior antibiotics. Before start of RT 20.8% had cultures positive for gram negative bacilli (GNB) increasing to 50.0% with positive cultures at the end of RT. 8 weeks after RT 33.3% had cultures positive for GNB. A total of 75% had cultures positive for GNB during the testperiod. Among these, 67% had received prior antibiotics.

Among the group of patients who developed cultures differing from normal flora during the first half of RT the median time to development of erythema grade 3 was 107 days compared to 43.5 days for patients with normal flora ($p = 0.07$). A trend towards earlier development of mucositis ($p = 0.103$ for grade 1 and $p = 0.232$ for grade 2) in patients with pathogenic cultures was found.

Conclusions: Among patients with cultures positive for GNB the majority had received prior antibiotics. Development of cultures positive for yeast was not associated with prior antibiotic therapy, and seems to be secondary to RT-induced mucositis. A possible correlation between toxicity of RT and pathogenic flora was detected.

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A comparative analysis between Ho's and UICC classification for nasopharyngeal carcinoma (NPC)

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Purpose: Ho's classification differs in some aspects of UICC staging: T1 Ho = T2&2 UICC; N category defines the level of nodal involvement (dimension for UICC); st V delineates hematogenous spread. The aim of the study is a comparison Ho v UICC classification.

Methods: Between 1987–95, 374 NPC pts were treated with radiotherapy (RT) (277 pts) or chemotherapy (BEC) followed by RT (97 pts), with no differences in survival (S) or disease free-survival (DFS). Kaplan-Meier method was used for actuarial S, DFS and freedom from distant metastasis (FDM) and log-rank method to test differences.

Results: 239 (64%) men, age 47 [8–78], histology (WHO): I v II v III: 76 v 36 v 262 pts. Stage distribution UICC/Ho: I 5/19, II 14/87, III 36/182, IV 319/80, V 0/6, shows an overcrowded st IV UICC versus (v) a well balanced Ho classification. *Overall S* (3y): st I v II v III v IV: 80% v 61% v 41% v 33% (Ho); I&II 80% v III 74% v IV 41% (UICC). *DFS:* st I v II v III v IV: 81% v 66% v 44% v 32% (Ho); I&II 81% v III 73% v IV 43% (UICC). There was a significant difference in S and DFS ($p < 0.01$) between Ho's stages in most comparisons (I v III, I v IV; II v III, II v IV). For UICC, only comparisons with